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CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

GUIDELINES FOR OUTPATIENT INTRAVENOUS UPLIZNA (INEBILIZUMAB-CDON) THERAPY

Section: Nursing
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
TJC Standards: N/A
Policy ID: NUR252
Effective: 1/3/23
Reviewed:
Revised:
Approved by: Kathleen Patrick, President, 1/3/23

I. BACKGROUND

Uplizna (inebilizumab) is a humanized IgG monoclonal antibody directed against CD19. The precise mechanism by which inebilizumab exerts its therapeutic effects in neuromyelitis optica spectrum disorder (NMOSD) is unknown. It is presumed to involve binding to CD19, a cell surface antigen presents on both immature and mature B lymphocytes. Following cell surface binding to B lymphocytes, inebilizumab results in antibody-dependent cellular cytolysis. The following outlines the procedures for servicing patients in need of outpatient intravenous (IV) inebilizumab infusions.

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:
   1. Prescriber preference
      a. Allergy profile
      b. Age $\geq$ 18 years old
      c. Ability to secure contracted nursing for subsequent infusions
      d. Other relevant social and/or medical history

C. Physician orders for inebilizumab must include:
   1. Drug and dose

2. Route of administration
3. Frequency of administration
4. Line care protocol
5. Emergency medications
6. Orders for IV corticosteroid, oral (PO) antihistamine, and PO antipyretic or equivalent per guidance from the prescribing information (PI). Refer to PI for examples, dosing ranges, and pre-medication administration windows.

D. Baseline labs or tests prior to starting therapy
    1. TB screening/test (both active and latent)
    2. Hepatitis B virus (HBV) screening
    3. Quantitative serum immunoglobulins

E. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See policy NUR012 (Appendix A).

III. PHARMACOLOGY OVERVIEW

Refer to manufacturer's full Prescribing Information for must up to date information.

A. Dosage and Indications
    1. Neuromyelitis optica spectrum disorder: adults who are anti-aquaporin-4 (AQP4) antibody positive
        a. Initial
            i. 300mg IV infusion on day 1, followed by 300mg IV infusion 2 weeks later
        b. Maintenance
            i. 300mg IV infusion every 6 months, starting 6 months after the first 300mg dose

B. Dose Adjustments
    1. No dose adjustments are listed in the package insert.

C. Duration
    1. Duration of therapy should be dependent on patient response and adverse reaction
    2. No specific duration is noted in the package insert

D. Contraindications
    1. Previous life-threatening reaction to infusion of inebilizumab
    2. Active hepatitis B infection
    3. Active or untreated latent tuberculosis

E. Warnings and Precautions
    1. Infusion reactions
        a. Administer pre-medications prior to infusion. Other management recommendations depend on the type and severity of the reaction.
        b. Permanently discontinue inebilizumab if a life-threatening or disabling infusion reaction occurs.
        c. Less severe infusion reactions can be managed through temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.
    2. Infections
        a. Possible increased risk of immunosuppressant effects with other immunosuppressants
            i. Inebilizumab has not been studied in combination with other immunosuppressants. If another immunosuppressant is initiated, consideration should be given to the potential for increased immunosuppressive effects
        b. Hepatitis B virus (HBV) reactivation
            i. Risk of HBV reactivation has been observed with B-cell depleting antibodies.
            ii. Inebilizumab should not be administered to patients with active hepatitis.
            iii. Screen patients for HBV before initiation of treatment with inebilizumab
        c. Progressive multifocal leukoencephalopathy (PML)
            i. PML has been observed in patients treated with B-cell depleting antibodies.
            ii. Inebilizumab should be held if signs or symptoms of PML are present
        d. Tuberculosis (TB)
            i. TB risk factors should be evaluated, and patients tested for latent TB infection prior to inebilizumab initiation.
            ii. Anti-TB therapy prior to initiation of inebilizumab should be considered in patients with risk factors and those with a history of latent TB infection with no confirmed treatment course.
        e. Vaccinations
            i. All necessary vaccinations should be completed at least 4 weeks prior to initiation of inebilizumab therapy.
            ii. Vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation, until B-cell repletion.
        f. Delay inebilizumab administration in patients with an active infection until the infection is resolved
    3. Immunoglobulin levels

a. Monitor immunoglobulin levels at the beginning, during, and after discontinuation of treatment until B-cell repletion.
b. Consider discontinuation of inebilizumab if a patient with low immunoglobulin G or M develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with IV immunoglobulins.

4. Fetal risk
    a. May cause fetal harm based on animal data.
        i. Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other B-cell depleting antibodies during pregnancy.
    b. Advise females of reproductive potential of the potential risk to a fetus and counsel to use an effective method of contraception during treatment and for 6 months after stopping inebilizumab.

F. Pharmacokinetics
1. Vd (central): 2.95L; Vd (peripheral): 2.57L
2. Metabolism: degraded by proteolytic enzymes widely distributed in the body
3. T ½: 18 days

G. Adverse Reactions
1. > 10%
    a. Urinary tract infections
    b. Decreased neutrophils
2. 1%-10%
    a. Lymphocytopenia
    b. Antibody development
    c. Influenza infection
    d. Arthralgia, back pain
    e. Nasopharyngitis, upper respiratory tract infections
    f. Infusion related reactions
3. Undefined frequency
    a. Decreased serum immunoglobulins

H. Drug Interactions
1. Concurrent use of immunosuppressant drugs, including systemic corticosteroids, may increase the risk of infection.

IV. ADMINISTRATIVE GUIDELINES

A. Administration
1. IV infusions should be given immediately after dilution. Use within 1 hour of preparation per current USP Immediate-Use Guidelines.

B. Assess for active infection before each infusion
    1. In case of active infection, delay infusion of inebilizumab until the infection resolves

C. Pre-medicate with an antihistamine, antipyretic, and a corticosteroid 30-60 minutes prior to infusion.

D. Allow inebilizumab to reach room temperature before administration.
    1. Administer diluted infusion over about 90 minutes at an increasing rate every 30 minutes as described below in Nursing Procedure.
    2. Must use a low-protein binding 0.2 or 0.22 micron in-line filter.

E. Monitor for infusion reactions during therapy and **for at least 1 hour after infusion.**

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:
    1. Alcohol Swabs
    2. Gloves
    3. Inebilizumab drug vials
    4. Tape
    5. Port Access Needle (Ex: 22 Gauge x ¾" Safe step)
    6. IV injection cap
    7. Dressing change kit
    8. Administration tubing
    9. Extension set 8"
    10. IV start kit for peripheral line
    11. IV peripheral catheter (Ex: 24 Gauge x ¾" or 22 Gauge x 1")
    12. Pole mounted infusion pump
    13. IV pole and pole clamp
    14. Batteries for pump administration
    15. Syringes (10mL) with needles
    16. Bag of sodium chloride 0.9% for dilution (250mL)
    17. Normal Saline (0.9%) flushes
    18. Sharps container

B. How Supplied
    1. Intravenous infusion: One carton contains 3 single dose inebilizumab vials
    2. Injection vial: 100mg/10mL (10mg/1mL) as a clear to slightly opalescent, colorless to slightly yellow solution.

C. Storage and Handling
    1. Refrigerate at 2°C to 8°C (36°F to 46°F) in original carton to protect from light

2. Do not freeze
3. Do not shake
4. Store vials upright

D. Compatibility
   1. Dilution with 0.9% Sodium Chloride
   2. No compatibility tests for other intravenous agents currently exist

E. Procedures: Preparation of product, infusion rates, post infusion monitoring time.
   1. Explain the reasoning for visit and use of inebilizumab.
   2. Don gloves.
   3. Establish venous access prior to preparation of drug.
   4. Counsel patient on warnings, precautions, and potential side effects including but not limited to:
      a. Increased risk of infections
      b. Infusion reactions
   5. Counsel females of reproductive potential on risk of fetal harm and need to use effective contraception.
   6. Prepare Product
      a. Visually inspect inebilizumab solution for particulate matter and discoloration. If the solution is cloudy, discolored, or contains discrete particulate matter, do not use and contact the manufacturer. Do not shake the vial
      b. Obtain a 0.9% Sodium Chloride 250mL intravenous bag
      c. Withdraw 10mL of inebilizumab from each of the 3 vials contained in the carton and transfer a total of 30mL into the 250mL NS intravenous bag.
      d. Mix diluted solution by gentle inversion. Do not shake the solution.
      e. Discard the unused portion remaining in the vials.
   7. Infusion rates
      a. Prior to the start of the intravenous infusion, the prepared infusion solution should be at room temperature. Infuse with increasing rates to completion, approximately over 90 minutes

Elapsed Time (minutes)	Infusion Rate (mL/hour)
0-30	42
31-60	125
61 to completion	333

VI. CLINICAL MONITORING

A. Prior to therapy
   1. HBV screening
   2. Quantitative serum immunoglobulins

3. TB screening (active and latent)
4. Assess for active infection prior to each infusion
5. Confirmation of contraceptive use in female patients of reproductive potential
6. Ensure patient is up to date on all necessary vaccinations prior to start of treatment

B. During therapy
    1. Quantitative serum immunoglobulins
    2. Signs and symptoms of active TB
    3. Monitor for infusion reactions during therapy and **for at least 1 hour after infusion**
    4. Signs and symptoms of infection and PML

C. After discontinuation of therapy
    1. Quantitative serum immunoglobulins
    2. Signs and symptoms of active TB
    3. Signs and symptoms of infection and PML

Please refer to the package insert for the most up to date guidance on this medication.

REFERENCES:

A. Uplizna (inebilizumab) package insert. Deerfield, IL: Horizon Therapeutics; 2021 Jul.
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C. Acheson EE, Acton J, Afolabi T, et al. "Inebilizumab: Drug Information." UpToDate. Accessed October 20, 2022. https://www.uptodate.com/contents/inebilizumab-drug-information?search=uplizna.
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APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS

Emergency Medication After Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

All other contents will not be needed.

Open the IM Epinephrine Bag

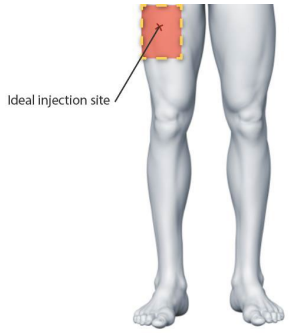
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampul use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampul of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an **alcohol swab, wipe the neck of the epinephrine ampul.**
3. Holding the ampul upright, **swirl and flick the ampul until all fluid flows to the bottom chamber** (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampul and with your other hand grasp the bottom chamber of the ampul. **Quickly snap the top of the ampul off, directing the snap way from you.**

5. **Place the tip of the brown filter needle inside the ampul**. Tilting the ampul, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampul and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
7. **Push the air out of the syringe by gently pushing on the plunger**.
8. Replace the cap on the brown filter needle. Discard remainder in ampul.
9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

Take the pills by mouth.

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.
Call 911 or have someone drive you to the emergency department.